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Transesophageal echocardiographic study of decompression-induced venous gas emboli

B. D. BUTLER and W. P. MORRIS

Department of Anesthesiology, The University of Texas-Houston Medical School, Houston, Texas 77030

Butler BD, Morris WP. Transesophageal echocardiographic study of decompression-induced venous gas emboli. Undersea Hyperbaric Med 1995; 22(2):117–128.—Transesophageal echocardiography was used to evaluate venous bubbles produced in nine anesthetized dogs following decompression from 2.84 bar after 120 min at pressure. In five dogs a pulsed Doppler cuff probe was placed around the inferior vena cava for bubble grade determination. The transesophageal echo images demonstrated several novel or less defined events. In each case where the pulmonary artery was clearly visualized, the venous bubbles were seen to oscillate back and forth several times, bringing into question the effect of coincidental counting in routine bubble grade analysis using precordial Doppler. A second finding was that in all cases, extensive bubbling occurred in the portal veins with complete extraction by the liver sinusoids, with one exception where a portal-to-hepatic venous anastomosis was observed. Compression of the bowel released copious numbers of bubbles into the portal veins, sometimes more than were released into the inferior vena cava. Finally, large masses of foam were routinely observed in the non-dependent regions of the inferior vena cava that not only delayed the appearance of bubbles in the pulmonary artery but also allowed additional opportunity for further reaction with blood products and for coalescence to occur before reaching the pulmonary microcirculation. These novel observations are discussed in relation to the decompression process.

transesophageal echocardiography, decompression, venous gas emboli, Doppler, dogs

Formation of venous gas emboli (VGE) as a result of decompression from hyperbaric or to hypobaric pressures is well recognized. Ever since the first use of ultrasound devices to detect microbubbles in blood with decompression, numerous attempts have been made to correlate the bubble signals with symptoms, with and without success (1–3). In many clinical situations the detection of VGE is critical; for example, in certain neurosurgical or cardiac cases (4). Although attempts have been made to quantitate the amount of intravascular gas in these situations, they are less often reported when compared to the diving situation. In the evaluation of decompression exposures there has been a great deal of effort expended in providing a semi-quantitative index of the amount of VGE formed

(2,5). These methods routinely employ precordial Doppler ultrasound including both pulsed and continuous-wave emitting devices.

In more recent years, echo imaging ultrasound devices including transesophageal echocardiography (TEE) have gained wider acceptance for use with VGE detection (6,7). Advantages of TEE include not only the ability to visualize and therefore localize the bubbles, as well as offer a greater degree of sensitivity (6), but also a greater opportunity to study some of the behavioral characteristics of intravascular bubbles. Using TEE, newer VGE classification schemes have been developed (8) which may offer some advantages over conventional Doppler, but cost and complexity constraints must be considered as well. Other uses of echocardiography are for detection of intracardiac defects (commonly a patent foramen ovale, PFO) in patients at risk for VGE (9) or with decompression (10).

The purpose of the present study was to evaluate and report on the use of TEE for detecting and characterizing VGE in anesthetized dogs after hyperbaric decompression. Much of what is reported, apart from the large quantities of circulating venous bubbles, represents some novel or at least less known observations about decompression-induced VGE. These observations and their potential impact on the evaluation of the decompression process are described.

METHODS AND MATERIALS

The procedures described in this study were approved by the Institutional Animal Care and Use Committee.

Anesthesia and surgery: Nine dogs (22–30 kg) were fasted for 12–24 h, anesthetized with intravenous pentobarbital sodium (30 mg · kg^{-1} and 5 mg · kg^{-1} · h^{-1}), intubated and ventilated with air at a rate (10–13 breaths/min) and tidal volume (15–20 ml/kg) to maintain end-tidal carbon dioxide (CO_2) at 35–40 mmHg. The dogs were supine and kept isothermic with a heated water blanket. Pressure-monitoring catheters were placed into the abdominal aorta via the right femoral artery for mean arterial pressure (MAP); the pulmonary artery via the right external jugular vein for pulmonary artery pressure (PAP), central venous pressure (CVP), and thermodilution cardiac output; and the left ventricle via the right carotid artery for left ventricular end-diastolic pressure (LVEDP). A venous catheter was placed into the inferior vena cava for fluid and anesthetic delivery. The pressure catheters were connected to calibrated pressure transducers, zero referenced to the right atrium. In five dogs a pulsed Doppler cuff probe (10 mHz) was placed around the inferior vena cava (5–20 cm below the TEE probe level) for audio recording of decompression-induced venous bubbles throughout the compression/decompression protocol. Bubble scores were made using a modification of the Spencer Code (5); designated continuous and peak bubble scores with and without deep-knee bends of the left hindlimb. Manipulation of the lower left leg consisted of full flexion, followed by compression.

Transesophageal echocardiographic (TEE) ultrasound imaging: TEE images were obtained using a biplane probe (5.3 mHz) and echocardiograph (Aloka 870). The probe was inserted into the esophagus (60–65 cm) for visualization of the inferior vena cava (IVC), hepatic and portal veins, pulmonary artery, and left atria and ventricle. The probe was initially positioned for viewing the IVC and hepatic vessels, then moved to the level of the heart. It was then intermittently repositioned between the sites throughout the experiment. Blood flow direction, velocity, and type (arterial vs. venous) were identified using color-flow Doppler. Biplane cross-sectional and longitudinal views as well as B- and M-mode records were videotaped for differentiation of venous bubbles.

Decompression procedures: After collection of baseline data, the animals were transferred to the experimental chamber, ventilated with a pressure-controlled, time-cycled ven-

tilator (Bird), and compressed to 2.84 bar (60 feet of sea water, fsw) at 0.37 bar/min (12 fsw/min) for a total bottom time of 120 min. The animals were then decompressed at 0.94 bar/min (30 fsw/min). After the decompression the animals were monitored for 120 min.

Statistical analysis was performed on the hemodynamic data using analysis of variance with Bonferroni correction for repeated measures.

RESULTS

Hemodynamics: The particular decompression exposure used in these studies was selected because of its relatively minimal effects on hemodynamics yet reproducible amounts of VGE formation. MAP, CVP, PAP, and LVEDP changes were nonsignificant compared to baseline, and all values were normalized within 120 min postdive.

Doppler ultrasound: Venous bubbles were first recorded from the IVC with the pulsed Doppler 8 ± 6 min (range 4–14 min) after the decompression to surface pressures in all dogs. Bubbles were recorded up to 120 min postdive. Bubble grades ranged from 1 to 3 for the continuous recordings, while four of five dogs demonstrated peak grades of 4, with deep knee bends for up to 90 ± 18 min (range 60–120 min postdive).

Transesophageal echocardiographic images

General bubble patterns: TEE images of venous bubbles were observed in all animals beginning 5 ± 2 min (range, 4–12 min) postdecompression (Fig. 1). The bubble patterns began slowly and reached peak levels approximately 25 min postdive. The bubble patterns then remained stable for 1–2 h (maximum observed was 195 min in one case), decreasing thereafter. The pulmonary artery was visualized in eight of nine dogs and showed bubble patterns consistent with the IVC images (Fig. 2). The bubbles were detected in the IVC, followed by the right atria, ventricle, and pulmonary arteries. No bubble images were observed in the left atria, ventricle, or aorta. TEE images of bubbles were not quantitated in terms of size or numbers.

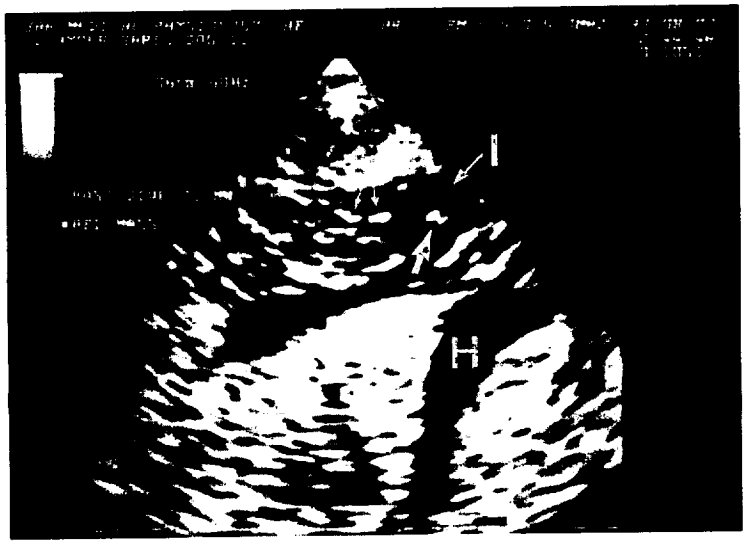

FIG. 1—Bubble images (*arrows*) within the inferior vena cava (horizontal dark area, *I*) 21 min postdive. Hepatic vein (*H*) is void of bubbles.

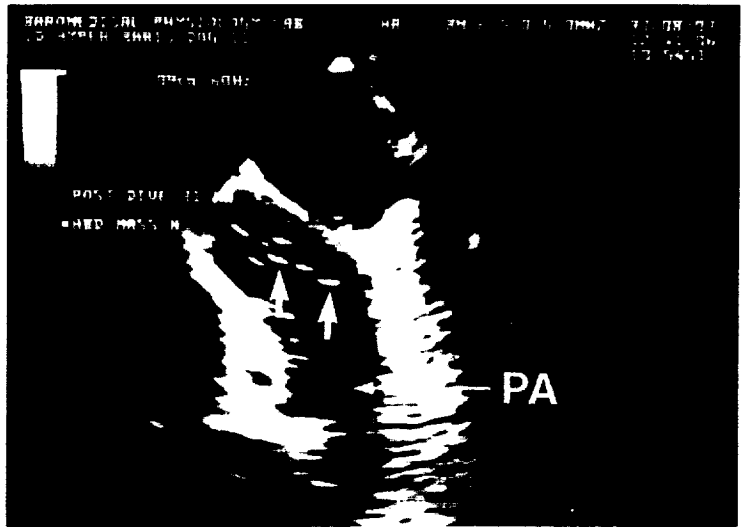

FIG. 2—Bubble images (*arrows*) in pulmonary artery (*PA*), traveling upward and to the left.

In addition to the above-described observations, we saw five additional phenomena of interest: a) accumulation of bubbles as a foam matrix in the non-dependent regions of the IVC, b) oscillatory motion of bubbles in the pulmonary artery, c) a preponderance of bubbles released from the bowel, d) portal venous bubbles with complete hepatic removal, and e) a single incidence of a portal-hepatic venous shunt.

Inferior vena cava bubble accumulation: In every experiment, gas bubbles were seen to accumulate as a foam-matrix in the non-dependent or lateral wall of the viewed segment of the IVC (Figs. 3 and 4). The images appeared as large echogenic segments with individual bubbles arriving at the caudal end (Fig. 3) and breaking off at the cranial end (Fig. 4). Manipulation of the vessel, or in one case advancing a balloon-tipped catheter (Fogarty) to the foam site, led to disintegration of the foam momentarily. The bubbles

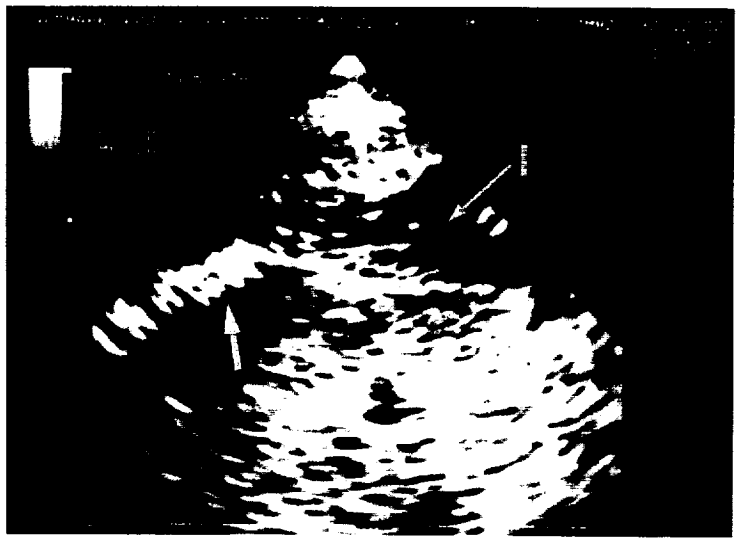

FIG. 3—Gas bubbles accumulating in inferior vena cava (*I*). *Note* bubbles being added to foam accumulation from lower left region (*large arrow*).

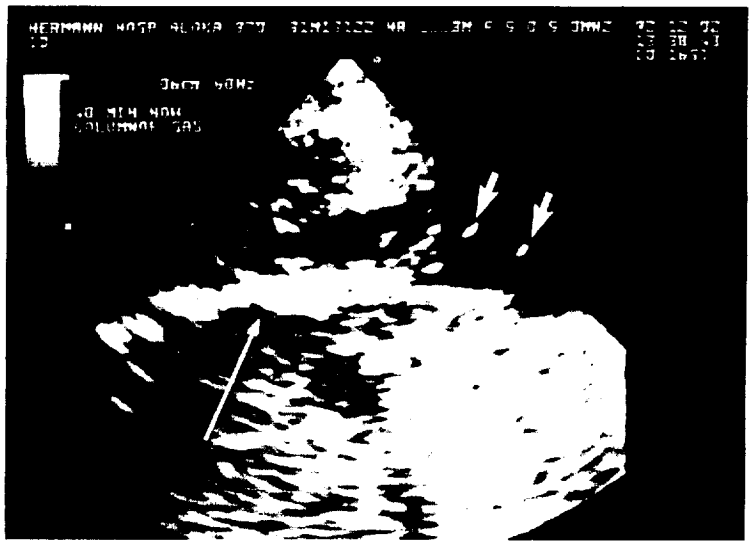

FIG. 4—Gas bubbles as foam matrix (*arrow*) in inferior vena cava. *Note* individual bubbles breaking off from right side (*small arrows*) and being carried away in flowing blood.

would then reaccumulate within 1–4 min. The foam accumulation never seemed to extend as far as the midregion of the vessel, and velocity (determined from Doppler recordings) did not seem to decrease significantly in the patent region of the IVC.

Bubble oscillations in the pulmonary artery: Where clear images of the pulmonary artery were obtained (7/9 cases), the movement of the bubbles did not seem to be continuous in the direction of the outflow tract but to be oscillatory in nature, dependent on the cardiac cycle. Examining numerous individual bubble movements revealed to and from oscillations that crossed an arbitrary line perpendicular to flow at least 2–3 times before progressing into the pulmonary branches. Eventually, usually within 3–7 cardiac cycles, the particular series of bubbles being imaged would clear the visual field and distribute into the pulmonary circulation. The movement of bubbles had a longer component in the forward direction. Blood velocity did not seem to be significantly impacted unless significant numbers of bubbles were present. Premature ventricular contractions tended to cause exaggerated oscillatory motion of the bubbles. Although this motion occurred in all cases where the pulmonary artery was visualized, it was not likely to have had a significant impact in interpreting any hemodynamic change because the amount of bubble formation was moderate (grade 3). On the other hand, significant numbers of VGE may reduce pulmonary artery blood flow and velocity, thereby increasing the effect of the oscillations on net bubble movement. These movements may also have an effect on the degree of reliability or accuracy of precordial Doppler used in deriving bubble scores based on relative count. Any coincidental or repetitive counting may lead to higher bubble scores than truly exist.

Bowel compression: It is commonly observed that flexion of a limb or increased physical activity will result in the release of decompression-induced VGE from capillary or small vessels into the greater venous circulation. These observations form the basis of using one of these activities when assessing bubble scores. Incidental to these findings (not unique to this report), we have observed that significant numbers of bubbles are also released into the IVC as a result of bowel compression, manipulation, or exaggerated respiratory maneuver simulating a Valsalva. In each of these situations large showers of bubbles were observed that qualitatively seemed to match or exceed those observed with individual hindlimb manipulation. The persistence of this source of venous bubbles did not seem to

last significantly longer than with limb flexion. Since all of the animals were fasted at least 12 h before decompression, it was not possible to determine if food intake had an influence on the amount of VGE released from the mesentery vessels upon bowel compression. In several cases the bowel compressions caused the release of showers of venous bubbles that were detected in the portal venous system. In at least one case where close scrutiny was maintained, hindlimb flexion failed to cause release of bubbles into the portal venous system whereas bowel compression did.

Portal venous bubbles: In each animal, decompression-induced VGE were imaged in the portal venous circulation. Figure 5 demonstrates images of portal venous gas. Appearance of portal venous bubbles was usually slightly delayed (1–5 min) as compared to IVC bubbles, although some variability may have been due to limb flexion or probe placement delays. In eight out of nine cases no bubbles were observed in the hepatic veins (Fig. 1) draining into the IVC. This apparently complete removal of portal venous bubbles (*see* one exception below) by the hepatic sinusoids seemed to be independent of the amount of gas bubbles or of relative size, assuming that the effective diameters may increase over time.

Portal-hepatic venous shunt: In one case, numerous gas bubbles were imaged post-decompression in both the portal veins and hepatic veins (Fig. 6). Upon closer examination a portal-hepatic venous shunt was detected (Fig. 7) that provided the anatomical route for the bubbles to bypass the hepatic sinusoids. Blood flow patterns and bubble distribution through the shunt were variable, according to the respiratory patterns, showing a predominance of bubble distribution in the direction of the hepatic vessels and ultimately the IVC.

DISCUSSION

The detection of decompression-induced gas bubbles has largely been restricted to intravascular bubbles and since the 1960s this has been accomplished using ultrasound devices. With transthoracic and TEE the VGE can be visualized for localization purposes, quantitation, or the study of their behavior in the circulation (4,11). Recent reports have described the use of echocardiography to study the relationship between serious decompression illness or paradoxical air embolism and a PFO in both clinical situations and with diving

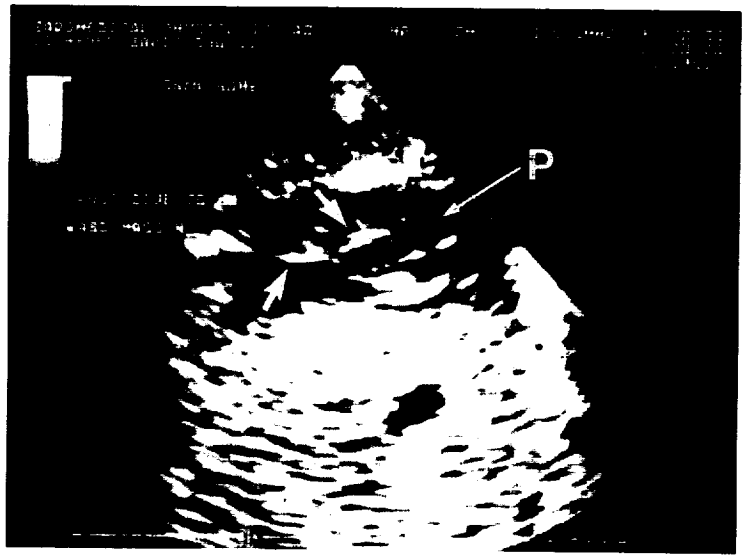

FIG 5—Collection of large and small bubbles (*arrows*) within portal vein (*P*).

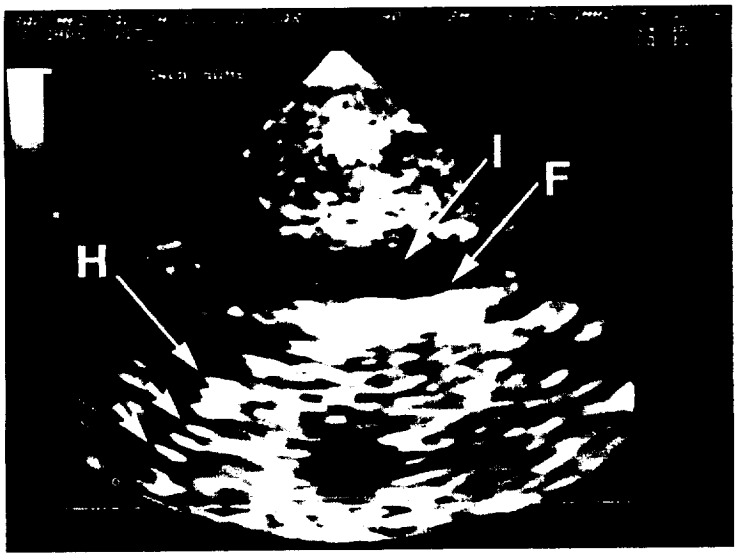

FIG. 6—Large number of bubbles in both inferior vena cava (*I*) (foam matrix *F*, bright white area) as well as bubbles arriving from hepatic vein (*H*, *small arrows*), *lower left*. This is from dog with portal-hepatic venous shunt.

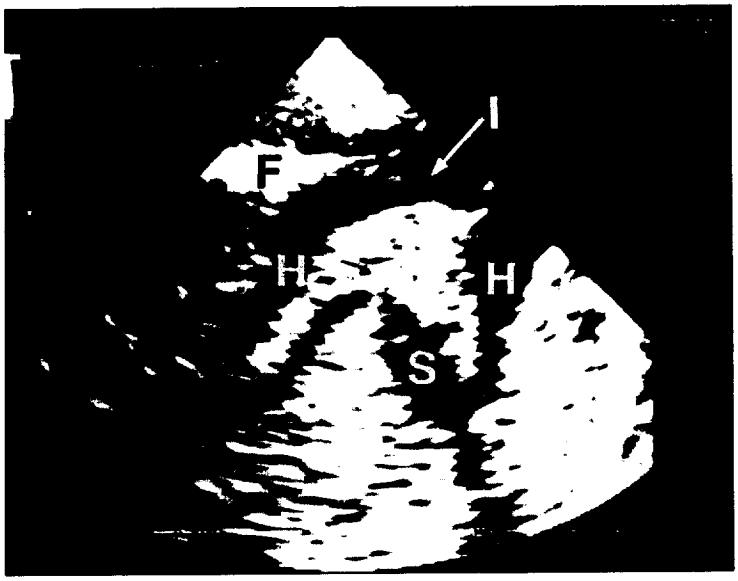

FIG. 7—Image of portal-hepatic venous shunt. Top horizontal vessel is inferior vena cava (*I*) with large foam collection (bright white area, *F*). Two hepatic veins (*H*) are entering IVC from the bottom, and shunt (*S*) connection with portal vein is seen between the two.

(7,12). Others have proposed the use of TEE not only for prospective screening for PFOs in patients at risk for VGE but also for perioperative monitoring and evaluation of air removal efforts in cardiac and neurosurgical cases (4,6,13).

Sensitivity of TEE for VGE detection was found to be superior to precordial Doppler, pulmonary artery pressure changes, and end-tidal carbon dioxide (6). In other reports, TEE was used to discriminate individual bubbles with diameters between 25 and 225 μm (mean 70 $\pm$ 49 μm) (14), which are within the size range of decompression bubbles (15).

Use of TEE for VGE detection also enables simultaneous Doppler monitoring of blood flow. In the present report we describe several novel findings regarding VGE detection with TEE after hyperbaric decompression.

Bubble accumulation in the inferior vena cava

The observation that VGE accumulate in the IVC is not surprising given the fact that previous reports have suggested that delays in appearance or prolongation of appearance of bubbles may be attributable to their adherence somewhere in the venous or capillary vessels (16). Their organization into a foam matrix was probably due to such factors as a) slower blood flow adjacent to the vessel walls, b) buoyancy with the slow flow and/or large bubble diameters, and c) possible surface tension effects (16). Also, because the blood flow in the IVC is less phasic than the pulmonary artery, there is a greater chance for bubble-to-bubble interaction and ultimately coalescence to occur (16).

Coalescence can occur during the accumulation phase in the IVC, thereby resulting in larger bubbles that are more likely to embolize the lungs and more stable bubbles that persist for longer periods of time. Any increase in the half life of the bubbles also enhances the likelihood that more blood-to-bubble interactions will occur, causing activation of cellular events (17,18) or release of bioactive compounds (19) that may play a role in the pathophysiology of decompression illness. Larger bubbles are also likely to have direct and prolonged contact with the lining of blood vessels, possibly resulting in endothelial damage and further cellular reaction.

The observance of VGE accumulating in the IVC began within the first few minutes postdecompression and persisted for 1–2 h. When the foam was cleared away with a balloon-tipped catheter, it reformulated over the subsequent 1–4 min. Further studies might examine the role of exaggerated respiratory or abdominal maneuvers in causing the release of large showers of VGE from IVC sites and the effect, if any, on pulmonary hemodynamics or the role of body position.

Pulmonary artery bubbles

Visualization or Doppler detection of decompression-induced VGE in the pulmonary artery is the principal advantage in the use of ultrasound to evaluate the decompression process. Since the venous blood flow reaches a confluency in the pulmonary artery, the precordial position is the optimal site for detection, although there are inherent difficulties associated with probe placement or baseline heart sounds. The results of this study suggest that the oscillatory motion of the bubbles in the pulmonary artery may raise additional questions regarding repeat or coincidental counting of bubbles when using ultrasound in the precordial position. These conditions may thereby result in overestimations of bubble scores in certain situations.

An additional problematic concern, common to ultrasonic evaluation of decompression VGE, is the normal movement of bubbles into and out of the field being ensonified, thereby causing a potential error in too rapid or too slow field sampling for bubble counting. Although it is difficult to ascertain what degree of inaccuracy these observations might impose on conventional bubble classification schemes (2,5), they do pose a new question that is often overlooked, especially where specific counting or sizing techniques are employed.

Portal venous gas bubbles

From the observation that all animals had portal venous bubbles we conclude that the liver is a significant target organ for decompression-induced VGE. Further, the fact that in all but one very unique case (*see* below; Portal to hepatic vein shunt) there were no hepatic bubbles observed, suggests that the liver can effectively remove significant amounts of bubbles from the venous circulation. Specific reporting of portal VGE with decompression is extremely rare. Gersh and Catchpole (20) described a few bubbles in only a few animal specimens, and a single case of a single bubble was reported with altitude decompression (21). The reasons for this scarcity of reporting may be that only until recently was real-time ultrasound imaging used with decompression evaluation as well as the delay and inherent difficulty in deciphering portal VGE with x-ray.

Concluding that the liver is a target organ for decompression-induced VGE is consistent with the same claim for the lungs, especially since both organs seem to exhibit similar spillover phenomena whereby large volumes of VGE cross their microcirculation, entering the pulmonary veins and left heart in the case of the lungs (22) or the IVC, right heart and pulmonary artery in the case of the liver (23). Root et al. (23) reported that with direct infusion of air into the portal vein of anesthetized dogs, portal venous pressure increased, systemic blood pressure decreased, and that a delay in appearance of bubbles in the systemic veins was possibly due to their being trapped in the portal venous system. In fact, only after 10–15 ml of air was infused directly into the portal vein were portal venous and systemic blood pressure noticeably changed. Because this volume probably represented a much greater amount of gas entering the splanchnic circulation than with decompression, it is not surprising that so few reports of liver damage are reported.

Clinical reports of portal venous gas primarily involve intestinal mucosal ulceration, septicemia, ulcerative colitis, bowel distension, and spreading cellulitis or abscess (24,25). The overall mortality rates in these cases are reportedly as high as 75–85% (24), although the cause is more likely to be the underlying etiologies (25) rather than the presence of the bubbles themselves in the portal veins.

The source of portal venous gas in the above clinical situations reportedly included bowel intraluminal gas being forced through the ulcerated mucosa or by significantly elevated intraluminal pressures (25). With decompression, an elevated intraluminal pressure or even an ulcerated mucosa cannot be ruled out entirely; however, it is more likely that the VGE detected in this study originated from the vasculature of the gastrointestinal tract, spleen, pancreas, and gallbladder or mesentery and were introduced into the portal veins in this situation, the same as they are reported elsewhere in the venous circulation with decompression.

The risk of portal venous gas itself may be limited to its effects on liver function. Any obstruction of portal flow, especially by microbubbles that react with the blood to cause further obstruction by denatured protein, fibrogen, platelets, etc. (17,18), may reduce or prevent first-pass hepatic detoxification (25) or alter the pharmacokinetics of adjunctive therapeutic agents. Changes in hepatic function after decompression, as expressed by changes in enzyme levels, have been reported with a high degree of variability. Jacey et al. (26) found no changes in glutamic oxalacetic transaminase (GOT) in a diver with joint pain and a nonsignificant elevation in alkaline phosphatase (ALP) 10 days after recompression therapy. Jauchem et al. (27) found no change in hepatic enzyme levels in VGE-susceptible and VGE-resistant individuals undergoing hypobaric decompression. Only in moderate-to-severe decompression illness did Freeman and Philp (28) report significant changes in GOT, ALP, or glutamic pyruvic transaminase (GPT) in rats as did Powell et al. (29) in guinea pigs, rats, and rabbits. Interestingly, Freeman and Philp (28) also evaluated hepatic enzyme changes with hypoxemia in the absence of bubbles, since their rats

demonstrated lung damage and labored breathing and found similar levels to those reported with decompression illness. Although these subsequent studies raise some questions about the role of tissue hypoxia in the changes in liver enzyme levels, there is little doubt that the combined effects of portal venous bubbles, reduction in blood volume reported with decompression, and blood-to-bubble interactions all combine to negatively impact the liver, at least in moderate to severe cases (28). Freeman and Philp (28) also reported on two divers (same dive), one of which developed severe symptoms of decompression illness while the other remained asymptomatic. Both showed elevated hepatic enzyme levels alternatively between 6 and 20 h postdive. In another report (18), the enzyme levels were elevated even in a diver manifesting joint pain only. Summarizing these reports it seems evident that the results of animal studies indicate that severe decompression illness, where hepatic embolization is not ruled out, is a prerequisite for liver damage, although several individual case reports raise the question of increased sensitivity in humans. Smith and Neuman (30) reported elevated levels of GOT and GPT in patients with arterial gas emboli, presumably due to hepatic artery embolization. The reason for the liver's tolerance to decompression-induced VGE is most likely due to the dual blood supply via the portal vein and hepatic artery, especially since the oxygen delivery is via the hepatic artery.

Portal vein to hepatic vein shunt

The appearance of bubbles in the hepatic veins is a rare occurrence. While VGE may be present in the portal veins, an extensive amount of gas must be present for there to be spillover of bubbles through the sinusoids into the hepatic veins (23). Alternatively, the central veins and hepatic sinusoids may become dilated with chronic right ventricular failure (31) or the perisinusoidal spaces can open as an agonal event (31). Portal-venous to hepatic-venous shunts are a rare occurrence that can be identified with duplex ultrasonography (32). The one incident of hepatic bubbles reported in the present study resembled the flow pattern described for similar events described by Tanaka et al. (32) for a portal-to-hepatic venous shunt.

Of the two earlier references describing the presence of hepatic bubbles with decompression, one described only a single hepatic bubble and it was not clear how far from the communication with the IVC the bubble appeared. This might be of importance, because on numerous occasions in the present study where we observed large numbers of IVC bubbles, individual or a few bubbles appeared to move retrograde into the first 1–2 cm of the connecting hepatic veins during the inflation phase of the respiratory cycle. These bubbles would be confused for hepatic venous bubbles if not for close observation of the blood flow patterns.

With all studies using ultrasound echocardiography, it is important to be able to discriminate gas microbubbles from other small echogenic particles normally present in large veins. These echoes, probably red cell aggregates (33), are usually of relatively low amplitude, are continuous with the blood flow, and are more obvious with slow flow. We did not observe these artifact echoes to increase in frequency or density after decompression, although there did appear to be considerable individual variability among the animals. Gain setting adjustment on the echo device usually enables the operators to diminish their visibility and therefore more carefully identify newer or different echogenic material.

The results of this report further demonstrate the utility of TEE in the evaluation of the decompression process and raise several new questions regarding the role of intravascular gas bubbles in decompression illness.

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